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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :

ROB HOOFT VAN HUIJSDUIJNEN, ET AL. : EXAMINER: WEBB

SERIAL NO: 10/590,808 :

FILED: JANUARY 12, 2007 : ART UNIT 1612

FOR: USE OF METHYLENE AMIDE

DERIVATIVES IN

CARDIOVASCULAR DISORDERS

APPEAL BRIEF

COMMISSIONER FOR PATENTS ALEXANDRIA, VIRGINIA 22313

SIR:

This Brief appeals the final rejection of November 14, 2008. A timely Notice of Appeal was filed on May 13, 2009. A one-month extension of time request is filed with this Brief.

REAL PARTY IN INTEREST

The real party in interest is Applied Research Systems ARS, Curacao, Netherlands Antilles (Assignment recorded on July 2, 2007 at Reel/Frame 019506/0316).

RELATED APPEALS AND INTERFERENCES

There are no applications, patents, appeals, or interferences known to appellants, the appellants' legal representative, or the appellants' assignee which may be related to, directly affect, or be directly affected by or have a bearing on the Board's decision in the pending appeal.

STATUS OF CLAIMS

Claims 1-16, 20 and 21 are active.

Claim 17-19 have been cancelled. Claims 1-16, 20 and 21 are being appealed.

STATUS OF AMENDMENTS

There have been no amendments submitted that have not been entered into the record.

SUMMARY OF CLAIMED SUBJECT MATTER

The subject matter defined by claim 1, which is the only independent claim on appeal, is outlined below with reference to exemplary support in the originally filed application:

A method of treating coronary obstruction or peripheral vasoconstriction in a patient in need thereof, [page 5, lines 2-8 and page 36, lines 6-26] the method comprising

[page 10, lines 1-6]

administering an effective amount of a methylene amide of Formula (I) to treat coronary obstruction or peripheral vasoconstriction in the patient [page 5, lines 2-8 and page 36, lines 6-26]:

as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and its racemate forms, as well as pharmaceutically acceptable salts and pharmaceutically active derivatives thereof, [page 10, lines 1-6]

wherein

 R^1 is selected from the group consisting of (C_1-C_{15}) alkyl, (C_2-C_{12}) alkenyl, (C_2-C_{12}) alkynyl, aryl, heteroaryl, (3-8-membered)-cycloalkyl or heterocycloalkyl, (C_1-C_{12}) alkylaryl or (C_1-C_{12}) alkyl-heteroaryl, (C_2-C_{12}) alkenyl-aryl or -heteroaryl, (C_2-C_{12}) alkynyl-aryl and -heteroaryl; *[page 10, lines 9-16]*

 R^{2a} and R^{2b} are each independently from each other selected from the group consisting of H and (C_1-C_{12}) alkyl; *[page 10, lines 17-19]*

Cy is selected from D and E; [age 10, line 20]

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D is selected from the group consisting of thienyl and phenyl, each substituted with a phenyl, oxadiazole; or 1 or 2 moieties selected from the group consisting of -NH-CO-R³, - SO₂-NR³R³′, and -CO-NR³R³′; [page 10, lines 21-23]

E is selected from the group consisting of aryl, heteroaryl, (3-8-membered)-cycloalkyl and heterocycloalkyl wherein aryl, heteroaryl, (3-8-membered)-cycloalkyl and heterocycloalkyl are substituted by (C₂-C₁₈)alkynyl; *[page 11, lines 4-6]*

 R^3 , R^3 are independently selected from the group consisting of H, (C_1-C_{15}) alkyl, (C_2-C_{12}) alkenyl, (C_2-C_{12}) alkynyl, aryl, heteroaryl, (3-8-membered)cycloalkyl or heterocycloalkyl, (C_1-C_{12}) alkyl aryl or heteroaryl, (C_2-C_{12}) alkenyl-aryl or -heteroaryl, (C_2-C_{12}) alkynyl-aryl or -heteroaryl *[page 10, lines 23-26]*.

There is no step plus function or means-for limitation in claim 1.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claim 1-16, 20 and 21 are rejected under 35 USC 103(a) as being unpatentable over Liu et al (U.S. 2002/0025126) in view of Sowers et al (Hypertension 2001) and Parissis (International Journal of Cardiology, 2002) as set forth in the final Office Action of November 14, 2008.

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ARGUMENT

A. <u>The Examiner's rejection</u>

In the Office Action (OA) dated November 14, 2008, the Examiner rejected all of the pending claims in view of Liu in view of Sowers (*Hypertension* 2001) and Parissis (*Int J Cardio* 2002).

B. <u>Examiner's claim interpretation</u>

The Examiner did not present an interpretation of the claims.

Nonetheless, as apparent in the claims submitted, the invention is to a method of treatment of coronary obstruction or peripheral vasoconstriction using compounds of Formula (I). This treatment is independent of whether or not the patient has diabetes.

The invention is based on the *in vivo* data provided on pages 40-41 of the specification, using the coronary artery occlusion model of example 1 wherein mouse are not required to have diabetes.

C. The Examiner's findings of the scope and content of the prior art

The Examiner found that

Liu teaches compounds of formula (I). (OA at page 2).

Liu does not teach the treatment of coronary obstruction or peripheral vasoconstriction as required in the claims.

Sowers and Parissis are relied upon for their teachings correlating cardiovascular disease with diabetes (Sowers) and vasoconstriction with hypertension (Parissis).

More particularly, the Examiner alleges that treating diabetes would also treat hypertension and cardiovascular diseases, which are associated to diabetes based primarily on the disclosure in Sowers that: "each pathophysiological disease entity, although independent in its own natural history, serves to exacerbate the other."

Appellants have reviewed the cited portions of Sowers and reread Sowers's entire disclosure. Appellants fail to understand how the Examiner's findings with respect to the scope and content of the prior art, whether supported by Sowers or any other teaching in the cited art, relate to the subject matter Appellants claim and/or would have led a person having ordinary skill in the art to the claimed subject matter. The Examiner has not established that the prior art describes or reasonably would have suggested the use of compounds of formula (I) for the specific treatment of coronary obstruction and peripheral vasoconstriction.

The Office has the initial burden of proof to establish the prima facie obviousness of the subject matter Appellants claim in view of the prior art teaching. *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). Absent evidence which supports a rejection of the subject matter Appellants claim for obviousness, the Examiner's conclusion that Appellants' claims are unpatentable under 35 U.S.C. §103(a) must be withdrawn. As explained further below, the combination of art cited in the rejection does not establish that there would have been a reasonable expectation of success without first having had performed the experiments shown in the present specification. The missing evidence from the cited publications must therefore lead only to the conclusion that the claims were not obvious. Once this data was available, and only then, could one have a reasonable expectation of success that compounds within the scope of the claims would work for the treatment of coronary obstruction or peripheral vasoconstriction.

The Examiner has not established that the prior art describes or reasonably would have suggested the use of Liu's compounds in very distinct treatments such as those from the claims.

D. The Examiner's view of the differences between the prior art and claimed processes

The Examiner finds that while Liu does not treat the indications in the claims "Sowers teaches "hypertension and endothelial dysfunction are strongly associated with diabetes patients" and that "each of these diseases serves to exacerbate the other." (OA at page 3).

- a) Sowers describes on page 1053, second column, that 'hypertensive patients who were taking beta blockers had 28% higher risk of diabetes than did those taking no medication". Similarly, Sowers reports end of page 1053 that "no reduction in progression to diabetes on ACE inhibition therapy was observed". This clearly demonstrates that the treatment of one disease does not necessarily positively impacts the other, and can even have a negative outcome on the progression of the other disease.
- b) Sowers discloses on page 1054, end of first column that "the relative benefit on CVD risk reduction was conferred in a far more powerful fashion by intensive blood pressure reduction rather than by tight glucose control." This clearly demonstrates that an antidiabetic treatment would have no direct effect on cardiovascular diseases and teaches away from one skilled in the art to use an antidiabetic treatment to treat a cardiovascular disease.
- c) Sowers teaches that in the specific case of diabetic patients, cardiovascular diseases may be more difficult to treat with common drugs than in the general case (see page 1054, end of first paragraph: "again, diabetic patients required more antihypertensive treatment to achieve goal blood pressure" and page 1054 second paragraph: "The necessity for use at least 3 drugs for tight control was also observed in the diabetic cohorts"). This does not provide any indication that using an antidiabetic agent would also treat cardiovascular diseases.

Persons having ordinary skill in the art normally seek "to improve upon what is already generally known." *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003). However, before persons having ordinary skill in the art would want to improve upon earlier methods of treating coronary obstruction or peripheral vasoconstriction with a different class of drug, the prior art must provide a reasonable expectation of success. Here, the prior art of Liu, Sowers

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and Parissis does not do that. In fact, the only suggestion to do what Appellants have done is Appellants own disclosure, i.e. hindsight. Hindsight reconstruction using only Appellants' disclosure to piece together cited references is, however, strictly prohibited. See M.P.E.P. § 2145. X.A.; see also KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 82 USPQ2d 1385 (2007). (internal citations omitted) ("[a] factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning.")

Where, as here, the rejection of the subject matter Appellants claim is based on hindsight, the rejection is improper. *In re Fritch*, 972 F.2d at 1266; *In re Fine*, 837 F.2d at 1075.

E. The Examiner's conclusion of obviousness

The Examiner states that, in light of his findings of the prior art:

It would have been obvious to a person having ordinary skill in the art at the time of applicant's invention to administer the compounds of Liu for the treatment of coronary obstruction and peripheral vasoconstriction, since they are problems associated with diabetes. Administering the compounds of Liu to diabetic patients with atherosclerosis and/or hypertension would also treat coronary obstruction and peripheral vasoconstriction.

OA at page 3

The significance of the Examiner's conclusion can be understood only when it is considered in light of the wealth of clearly erroneous findings which immediately precede it. Consider the statement in context (OA, p. 3):

Since they [coronary obstruction and peripheral vasoconstriction] are problems associated with diabetes.

The Examiner's apparent finding is clearly erroneous. Although Sowers establishes that ACE inhibitors may impact the progression of diabetes (see in particular HOPE trial on

page 1055) Sowers does not provide any indication as whether an antidiabetic agent, like the compounds of the present application, would impact cardiovascular diseases.

Additionally, Sowers explains the effect of ACE inhibitor to diabetes at the cellular level, through a specific pathway involving angiotensin II and Pi3K (see on page 1056 second paragraph). These biological entities are completely distinct from PTP1 B, which is the biological target of the compounds of the present application.

In fact, as discussed above in section D a), b) and c), Sowers rather teaches that the treatment of one disease does not necessarily positively impact the other, and can even have a negative outcome on the progression of the other disease. Further an antidiabetic treatment would have no direct effect on cardiovascular diseases and teaches away from one skilled in the art to use an antidiabetic treatment to treat a cardiovascular disease.

Finally, the Examiner's finding that "[a]dminstering the compounds of Liu to diabetic patients with atherosclerosis and/or hypertension would also treat coronary obstruction and peripheral vasoconstriction" at page 3 of the OA is clearly erroneous.

The aim of the Sowers' publication is to treat cardiovascular diseases associated with diabetes, using known antihypertensive agents. Sowers does not provide any hint to use an antidiabetic agent to treat cardiovascular diseases. Moreover, Sowers clearly teaches away one skilled in the art to use such an agent, as discussed in the section D a). Therefore, based on the teaching of Sowers, one skilled in the art would not have had any reasonable expectation of success in treating coronary obstruction or peripheral vasoconstriction, using an antidiabetic agent like compounds of formula (I) from Liu, as currently claimed. The conclusion of obviousness ignores that protease genes, while sharing a name and generalized activity, say nothing to their role in the cellular metabolism, machinery and survival. See also "To the extent an art is unpredictable, as the chemical arts often are, KSR's focus on these "identified, predictable solutions" may present a difficult hurdle because potential

solutions are less likely to be genuinely predictable." Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd,

533 F.3d 1353, 87 U.S.P.Q.2d 1452 (Fed. Cir. 2008).

Conclusions of obviousness based on clearly erroneous findings, as is here the case,

cannot stand. Alza Corp. v. Mylan Labs., Inc., 464 F.3d 1286, 1289 (Fed. Cir. 2006).

CONCLUSION

Appellants respectfully submit that the Examiner has not satisfied the Office's initial

burden to establish that the claims of this application are unpatentable under 35 U.S.C.

§103(a). The Examiner has erred in determining the scope and content of the prior art

teaching, erred in ascertaining the differences between the prior art and the claimed

invention, and based on the accumulated error, erred in concluding that the subject matter

Appellants claim is unpatentable under 35 U.S.C. §103(a) for obviousness at the time the

invention was made to a person having ordinary skill in the art in view of Liu in view of

Sowers (Hypertension 2001) and Parissis (Int J Cardio 2002).

For the reasons stated herein, Appellants respectfully request that the Examiner's

rejection under 35 U.S.C. §103(a) be withdrawn.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,

MAIER & NEUSTADT, P.C.

Daniel I Pereira, Ph.D.

Registration No. 45,518

Customer Number

22850

Tel: (703) 413-3000 Fax: (703) 413 -2220

(OSMMN 08/07)

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CLAIMS APPENDIX

Claim 1 (Rejected): A method of treating coronary obstruction or peripheral vasoconstriction in a patient in need thereof, the method comprising administering an

effective amount of a methylene amide of Formula (I) to treat coronary obstruction or peripheral vasoconstriction in the patient:

as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and its racemate forms, as well as pharmaceutically acceptable salts and pharmaceutically active derivatives thereof, wherein

 R^1 is selected from the group consisting of (C_1-C_{15}) alkyl, (C_2-C_{12}) alkenyl, (C_2-C_{12}) alkynyl, aryl, heteroaryl, (3-8-membered)-cycloalkyl or heterocycloalkyl, (C_1-C_{12}) alkyl-aryl or (C_1-C_{12}) alkyl-heteroaryl, (C_2-C_{12}) alkenyl-aryl or -heteroaryl, (C_2-C_{12}) alkynyl-aryl and -heteroaryl;

 R^{2a} and R^{2b} are each independently from each other selected from the group consisting of H and (C_1-C_{12}) alkyl;

Cy is selected from D and E;

D is selected from the group consisting of thienyl and phenyl, each substituted with a phenyl, oxadiazole; or 1 or 2 moieties selected from the group consisting of -NH-CO-R³, - SO₂-NR³R³', and -CO-NR³R³';

E is selected from the group consisting of aryl, heteroaryl, (3-8-membered)-cycloalkyl and heterocycloalkyl wherein aryl, heteroaryl, (3-8-membered)-cycloalkyl and heterocycloalkyl are substituted by (C_2-C_{18}) alkynyl;

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 R^3 , R^3 are independently selected from the group consisting of H, (C_1-C_{15}) alkyl, (C_2-C_{12}) alkenyl, (C_2-C_{12}) alkynyl, aryl, heteroaryl, (3-8-membered)cycloalkyl or heterocycloalkyl, (C_1-C_{12}) alkyl aryl or heteroaryl, (C_2-C_{12}) alkenyl-aryl or -heteroaryl, (C_2-C_{12}) alkynyl-aryl or -heteroaryl.

Claim 2 (Rejected): The method according to claim 1 wherein R^{2a} and R^{2b} are each H.

Claim 3 (Rejected): The method according to claim 1 wherein Cy is D.

Claim 4 (Rejected): The method according to claim 1 wherein R^{3'} is H and R³ is selected from the group consisting of diphenyl-ethyl, dodecyl, octyl, 4-pentyl-benzyl, 4-phenoxy-phenethyl, ethyl-thiophen-2-yl, pentadecyl, tridecyl, hexyloxy-phenyl or (2-ethyl)-hexyl.

Claim 5 (Rejected): The method according to claim 1 wherein Cy is E.

Claim 6 (Rejected): The method according to claim 5 wherein E is selected from the group consisting of phenyl, pyridinyl, naphthyl or benzofuranyl group, being substituted by B-R⁴ wherein B is ethynyl group and R⁴ is selected from the group consisting of (C₆-C₁₆)alkyl, (3-8 membered) cycloalkyl, (C₁-C₁₂)alkyl-(3-8 membered) cycloalkyl, phenyl or (C₁-C₁₂)alkyl phenyl.

Claim 7 (Rejected): The method according to claim 6 wherein E is phenyl substituted by $B-R^4$ wherein B is ethynyl group and R^4 is (C_6-C_{16}) alkyl.

Claim 8 (Rejected): The method according to claim 1 wherein R¹ is a moiety –CH₂-A, or -CH₂-CH₂-A wherein A is selected from the group consisting of aryl, heteroaryl, (3-8-membered)heterocycloalkyl or (3-8-membered)cycloalkyl.

Claim 9 (Rejected): The method according to claim 1 wherein R¹ is A, wherein A is selected from the group consisting of aryl, heteroaryl, (3-8-membered)heterocycloalkyl or (3-8-membered)cycloalkyl.

Claim 10 (Rejected): The method according to claims 8 or 9, wherein A is selected from the group consisting of phenyl, pyridinyl, benzo-1,3-dioxolenyl, biphenyl, naphthyl, quinoxalinyl, thiazolyl, thienyl, furanyl or a piperidinyl group, optionally substituted by 1 or 2 cyano, halogen, NO₂, (C₁-C₆)alkoxy, aryloxy or heteroaryloxy, (C₁-C₆)thioalkoxy, (C₁-C₁₂)alkyl, (C₁-C₁₂)alkyl-X wherein X is halogen, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, aryl, heteroaryl, (3-8 membered) cycloalkyl or heterocycloalkyl, (C₁-C₁₂)alkyl aryl or heteroaryl, (C₂-C₁₂)alkenyl aryl or heteroaryl, (C₂-C₁₂)alkynyl aryl or heteroaryl, -COR³, -COOR³, -COOR³, -NHCOR³ wherein R³ is a (C₁-C₁₂)alkyl or (C₁-C₁₂)alkenyl, -SOR³, -SO₂R³, -SO₂NR³R³ with R³, R³ independent from each other and selected from the group consisting of H, straight or branched (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, aryl, heteroaryl, (3-8-membered)-cycloalkyl or heterocycloalkyl.

Claim 11 (Rejected): The method according to claim 1 wherein:

R^{2a} and R^{2b} are each H; R¹ is-CH₂-A, wherein A is phenyl or thienyl, optionally substituted by cyano, halogen, methoxy, hydroxy, phenoxy, -NO₂, trifluoromethyl; Cy is a

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thienyl, phenyl or biphenyl substituted by $-SO_2R^3$, $-CO-NR^3R^{3'}$ in which $R^{3'}$ is H and R^3 is (C_7-C_{12}) alkyl.

Claim 12 (Rejected): The method according to claim 1 wherein:

 R^{2a} and R^{2b} are each H; R^1 is— CH_2 -A, wherein A is phenyl or thienyl, optionally substituted by cyano, halogen, methoxy, hydroxy, phenoxy, -NO₂, trifluoromethyl; Cy is a thienyl, phenyl or biphenyl substituted by -SO₂R³, -CO-NR³R^{3'} in which R^{3'} is H and R³ is $(C_7$ - C_{15})alkyl.

Claim 13 (Rejected): The method according to claim 1 wherein the methylene amide is of Formula (I'):

wherein

 R^1 is selected from the group consisting of phenyl, benzyl, phenethyl, 1-methylbenzyl which is optionally substituted by (C_1-C_6) alkyl group or a cycloalkyl group; Cy is a phenyl or a biphenyl group substituted with a moiety selected from the group consisting of -NH-CO-R³, -CO-NH-R³, or an oxadiazole group substituted with R³, wherein R³ is (C_7-C_{15}) alkyl.

Claim 14 (Rejected): The method according to claim 13 wherein R³ is (C₈-C₁₅)alkyl.

Claim 15 (Rejected): The method according to claim 13 wherein R³ is dodecyl.

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Claim 16 (Rejected): The method according to claim 1 wherein the methylene
amide is selected from the group consisting of:
       (benzyl{4-[(dodecylamino)carbonyl] benzyl}amino)(oxo)acetic acid;
       oxo{{4-[(pentadecylamino)carbonyl]benzyl}[4-(trifluoromethyl)benzyl]amino}acetic
acid;
       (benzyl{4-[(pentadecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       (benzyl{4-[(tridecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       [benzyl(4-{[dodecyl(methyl)amino]carbonyl}benzyl)amino](oxo)acetic acid;
       {(4-{[dodecyl(methyl)amino]carbonyl}benzyl)[4-(trifluoromethyl)benzyl]amino}-
(oxo)acetic acid;
       ([1-(tert-butoxycarbonyl)-4-piperidinyl]{4-[(dodecylamino)carbonyl]benzyl}-amino)-
(oxo)acetic acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[3-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
       ({[1-(tert-butoxycarbonyl)-4-piperidinyl]methyl} {4-[(dodecylamino)carbonyl]-
benzyl} amino)(oxo)acetic acid;
       oxo {[4-(tridecanoylamino)benzyl][4-(trifluoromethyl)benzyl]amino}acetic acid;
       [benzyl(4-{[4-(hexyloxy)benzoyl]amino}benzyl)amino](oxo)acetic acid;
       oxo{[4-(trifluoromethyl)benzyl][4-(10-undecenoylamino)benzyl]amino}acetic acid;
       oxo{{4-[(9E)-9-tetradecenoylamino]benzyl}[4-(trifluoromethyl)benzyl]amino}acetic
acid;
       {benzyl[4-(tridecanoylamino)benzyl]amino}(oxo)acetic acid;
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{{4-[(2-hydroxydodecyl)amino]benzyl}[4-(trifluoromethyl)benzyl]amino}-(oxo)-
acetic acid;
       oxo{[4-(trifluoromethyl)benzyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]-amino}-
acetic acid;
       {({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)[4-(trifluoromethyl)benzyl]amino}-
(oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}({1-[(4-methoxyphenyl)sulfonyl]-4-piperi-
dinyl} methyl)amino](oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(2-carboxy-1-phenylethyl)amino](oxo)acetic
acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(2-methoxy-1-methylethyl)amino](oxo)acetic
acid;
       (4-bromo {4-[(dodecylamino)carbonyl]benzyl}anilino)(oxo)acetic acid;
       ({4-[(dodecylamino)carbonyl]benzyl}anilino)(oxo)acetic acid;
       ([2-(3-chlorophenyl)ethyl]{4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[2-(3-methoxyphenyl)ethyl]amino}(oxo)acetic
acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[(d,l)-trans-2-phenylcyclopropyl]amino}-(oxo)
acetic acid;
       ([(d,l)-trans-2-(benzyloxy)cyclopentyl]{4-[(dodecylamino)carbonyl]benzyl}-amino)-
(oxo)acetic acid;
       ({4-[(dodecylamino)carbonyl]benzyl}-4-phenoxyanilino)(oxo)acetic acid:
       [{4-[(dodecylamino)carbonyl]benzyl}(1,2,3,4-tetrahydro-1-naphthalenyl)amino]-
(oxo) acetic acid;
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((1-benzyl-4-piperidinyl){4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[2-(4-phenoxyphenyl)ethyl]amino}(oxo)acetic
acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[2-(2-phenoxyphenyl)ethyl]amino}(oxo)acetic
acid;
       ((2-[1,1'-biphenyl]-4-ylethyl) {4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid;
       (([1,1'-biphenyl]-3-ylmethyl){4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid;
       (3-(benzyloxy) {4-[(dodecylamino)carbonyl]benzyl}anilino)(oxo)acetic acid;
       ([4-(benzoylamino)benzyl]{4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid;
       N-(carboxycarbonyl)-N-{4-[(dodecylamino)carbonyl]benzyl}-3-phenyl-beta-alanine;
       {{4-[(dodecylamino)carbonyl]benzyl}{4-(1,2,3-thiadiazol-4-yl)benzyl]amino}-(oxo)
acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(4-pentylbenzyl)amino](oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(1-phenylethyl)amino](oxo)acetic acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[1-(1-naphthyl)ethyl]amino}(oxo)acetic acid;
       (benzyl{3-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       {{3-[(dodecylamino)carbonyl]benzyl}[4-(methylsulfonyl)benzyl]amino}(oxo)acetic
acid;
       ((3-cyanobenzyl) {3-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       {{3-[(dodecylamino)carbonyl]benzyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
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[(4-chlorobenzyl)(3-{[(4-pentylbenzyl)amino]carbonyl}benzyl)amino](oxo)acetic
acid;
                             oxo\{[4-(\{[2-(2-thienyl)ethyl]amino\}carbonyl)benzyl][4-(trifluoromethyl)-benzyl]]
amino}acetic acid;
                              \{benzy | [(3'-\{[(2,2-diphenylethyl)amino]carbonyl\}[1,1'-biphenyl]-4-yl)methyl]-4-yl\}
amino} (oxo)acetic acid;
                              {(3-cyanobenzyl)[(3'-{[(2,2-diphenylethyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)}
methyl]amino}(oxo)acetic acid;
                               {(4-chlorobenzyl)[(3'-{[(2,2-diphenylethyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)
 methyl]amino}(oxo)acetic acid;
                               {[(3'-{[(2,2-diphenylethyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)methyl][4-(trifluoro-
 methyl)benzyllamino}(oxo)acetic acid;
                               ((3-cyanobenzyl)\{[3'-(\{[2-(4-phenoxyphenyl)ethyl]amino\}carbonyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)\{[3'-(\{[2-(4-phenoxyphenyl)ethyl]amino\}carbonyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanobenzyl)[1,1'-biphenyl]-4-((3-cyanob
 yllmethyl\amino)(oxo)acetic acid;
                              oxo\{\{[3'-(\{[2-(4-phenoxyphenyl)ethyl]amino\}carbonyl)[1,1'-biphenyl]-4-yl]methyl\}-1-yl]methyl\}-1-yl]methyl\}-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-1-yl[methyl]-
  [4-(trifluoromethyl)benzyl]amino}acetic acid;
                               [(3-cyanobenzyl)({3'-[(octylamino)carbonyl][1,1'-biphenyl]-4-yl}methyl)amino]-
  (oxo) acetic acid;
                                [(4-chlorobenzyl)({3'-[(octylamino)carbonyl][1,1'-biphenyl]-4-yl}methyl)amino]-
  (oxo) acetic acid;
                                 \{(\{3'-[(octylamino)carbonyl][1,1'-biphenyl]-4-yl\}methyl)[4-(trifluoromethyl)-benzyl]
  amino}(oxo)acetic acid;
                                  {(3-cyanobenzyl)[(3'-{[(3-phenylpropyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)
  methyl] amino}(oxo)acetic acid;
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       [(3-cyanobenzyl)({3'-[(dodecylamino)carbonyl][1,1'-biphenyl]-4-yl}methyl)-amino]-
(oxo)acetic acid;
       [(4-chlorobenzyl)({3'-[(dodecylamino)carbonyl][1,1'-biphenyl]-4-yl}methyl)-amino]-
(oxo)acetic acid;
       {({3'-[(dodecylamino)carbonyl][1,1'-biphenyl]-4-yl}methyl)[4-(trifluoromethyl)-
benzyl]amino}(oxo)acetic acid;
       {benzyl[(3'-{[(4-pentylbenzyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)methyl]amino}-
(oxo)acetic acid;
       {(3-cyanobenzyl)[(3'-{[(4-pentylbenzyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)-
methyl] amino}(oxo)acetic acid;
       {(4-chlorobenzyl)[(3'-{[(4-pentylbenzyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)-
methyl] amino}(oxo)acetic acid;
       oxo{[(3'-{[(4-pentylbenzyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)methyl][4-(trifluoro-
methyl)benzyl]amino}acetic acid;
       oxo{[(3'-{[(4-phenylbutyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)methyl][4-(trifluoro-
methyl)benzyl]amino}acetic acid;
       {(3-cyanobenzyl)[(3'-{[(2-mesitylethyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)-methyl]
amino}(oxo)acetic acid;
       {(4-chlorobenzyl)[(3'-\{[(2-mesitylethyl)amino]carbonyl\}[1,1'-biphenyl]-4-yl)-methyl]}
amino}(oxo)acetic acid;
       {[(3'-{[(2-mesitylethyl)amino]carbonyl}[1,1'-biphenyl]-4-yl)methyl][4-(trifluoro-
methyl)benzyl]amino}(oxo)acetic acid;
       ((4-chlorobenzyl){[3'-({[2-(4-methoxyphenyl)ethyl]amino}carbonyl)[1,1'-biphenyl]-
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[{4-[(dodecylamino)carbonyl]benzyl}(4-methoxybenzyl)amino](oxo)acetic acid;

4-yl]methyl}amino)(oxo)acetic acid;

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{{4-[(dodecylamino)carbonyl]benzyl}[4-(methylsulfonyl)benzyl]amino}(oxo)acetic
acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(4-methoxybenzyl)amino](oxo)acetic acid;
       {{3-[(dodecylamino)carbonyl]benzyl}[3-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
       ({4-[(dodecylamino)carbonyl]benzyl} {[6-(trifluoromethyl)-3-pyridinyl]methyl}-
amino)(oxo)acetic acid;
       4-[((carboxycarbonyl){3-[(dodecylamino)carbonyl]benzyl}amino)methyl]benzoic
acid;
       ({3-[(dodecylamino)carbonyl]benzyl}{4-[hydroxy(oxido)amino]benzyl}-amino)
(oxo) acetic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(2-fluorobenzyl)amino](oxo)acetic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(2-pyridinylmethyl)amino](oxo)acetic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(3-thienylmethyl)amino](oxo)acetic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(4-hydroxybenzyl)amino](oxo)acetic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(4-phenoxybenzyl)amino](oxo)acetic acid;
       ({3-[(dodecylamino)carbonyl]benzyl}{[6-(trifluoromethyl)-3-pyridinyl]methyl}-
amino)(oxo)acetic acid;
       3-[((carboxycarbonyl){3-[(dodecylamino)carbonyl]benzyl}amino)methyl]benzoic
acid;
       5-[((carboxycarbonyl){3-[(dodecylamino)carbonyl]benzyl}amino)methyl]-2-thio-
phenecarboxylic acid;
       ({4-[(dodecylamino)carbonyl]benzyl}{4-[hydroxy(oxido)amino]-benzyl}-amino)-
(oxo)acetic acid;
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((1,3-benzodioxol-5-ylmethyl){4-[(dodecylamino)carbonyl]-benzyl}amino)-(oxo)-
acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(2-fluorobenzyl)amino](oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(4-phenoxybenzyl)amino](oxo)acetic acid;
       4-[((carboxycarbonyl){4-[(dodecylamino)carbonyl]benzyl}amino)methyl]benzoic
acid;
       5-[((carboxycarbonyl) {4-[(dodecylamino)carbonyl]benzyl}amino)methyl]-2-
thiophene carboxylic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(2-thienylmethyl)amino](oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(isopropyl)amino](oxo)acetic acid:
       ((3,5-dichlorobenzyl){4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       [(3,5-dichlorobenzyl)(4-{[(3,3-diphenylpropyl)amino]carbonyl}-benzyl)amino]-(oxo)
acetic acid;
       [(4-{[(2-[1,1'-biphenyl]-4-ylethyl)amino]carbonyl}benzyl)(3,5-dichlorobenzyl)-
amino] (oxo)acetic acid;
       [(1,3-benzodioxol-5-ylmethyl)(4-{[(2-[1,1'-biphenyl]-4-ylethyl)amino]carbonyl}-
benzyl)amino](oxo)acetic acid;
       (2,3-dihydro-1H-inden-1-yl{4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid;
       {2,3-dihydro-1H-inden-1-yl[4-({[2-(4-phenoxyphenyl)ethyl]amino}-carbonyl)-
benzyl] amino}(oxo)acetic acid;
      [{4-[(dodecylamino)carbonyl]benzyl}(4-pyridinylmethyl)amino](oxo)acetic acid;
       ([4-(dimethylamino)benzyl] {4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid;
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[{4-[(dodecylamino)carbonyl]benzyl}(3-pyridinylmethyl)amino](oxo)acetic acid;

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((4-cyanobenzyl){4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(1,3-thiazol-2-ylmethyl)amino](oxo)acetic acid;
       ({4-[(dodecylamino)carbonyl]benzyl}{[2-(4-morpholinyl)-1,3-thiazol-5-yl]methyl}-
amino)(oxo)acetic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(4-pyridinylmethyl)amino](oxo)acetic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(3-pyridinylmethyl)amino](oxo)acetic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(3-hydroxybenzyl)amino](oxo)acetic acid;
       ((4-cyanobenzyl){3-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       [{3-[(dodecylamino)carbonyl]benzyl}(1,3-thiazol-2-ylmethyl)amino](oxo)acetic acid;
       ({3-[(dodecylamino)carbonyl]benzyl} {[2-(4-morpholinyl)-1,3-thiazol-5-yl]methyl}-
amino)(oxo)acetic acid;
       ((1,3-benzodioxol-5-ylmethyl){3-[(dodecylamino)carbonyl]-benzyl}amino)-(oxo)
acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(2-thienylmethyl)amino](oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(2-pyridinylmethyl)amino](oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(3-thienylmethyl)amino](oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(4-hydroxybenzyl)amino](oxo)acetic acid;
       3-[((carboxycarbonyl){4-[(dodecylamino)carbonyl]benzyl}amino)methyl]benzoic
acid;
       [cyclopentyl({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)aminol(oxo)acetic acid;
       [benzyl({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)amino](oxo)acetic acid;
       (({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl){3-[hydroxy(oxido)amino]-benzyl}-
amino)(oxo)acetic acid;
       [({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)(4-methoxybenzyl)amino]-(oxo)-
acetic acid;
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[({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)(2-fluorobenzyl)amino](oxo)acetic
acid;
       {({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)[4-(methylsulfonyl)-benzyl]-
amino}(oxo)acetic acid;
       [({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)(4-phenoxybenzyl)amino]-(oxo)-
acetic acid;
       4-{[(carboxycarbonyl)({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)-amino]-
methyl}benzoic acid;
       (({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl){[6-(trifluoromethyl)-3-pyridinyl]-
methyl}amino)(oxo)acetic acid;
       {({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)[3-(trifluoromethyl)benzyl]amino}-
(oxo)acetic acid;
       [(3-chlorobenzyl)({5-[(dodecylamino)sulfonyl]-2-thienyl}methyl)amino](oxo)acetic
acid;
       {[(5-{[(3,3-diphenylpropyl)amino]sulfonyl}-2-thienyl)methyl][3-(trifluoromethyl)-
benzyl]amino}(oxo)acetic acid;
       {(3-chlorobenzyl)[(5-{[(3,3-diphenylpropyl)amino]sulfonyl}-2-thienyl)methyl]-
amino}(oxo)acetic acid;
       oxo{{[5-({[2-(4-phenoxyphenyl)ethyl]amino}sulfonyl)-2-thienyl]methyl}[3-
(trifluoro-methyl)benzyl]amino}acetic acid;
       ((3-chlorobenzyl){[5-({[2-(4-phenoxyphenyl)ethyl]amino}sulfonyl)-2-thienyl]-
methyl}amino)(oxo)acetic acid;
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methyl)benzyl]amino}(oxo)acetic acid;

{[(5-{[(2-[1,1'-biphenyl]-4-ylethyl)amino]sulfonyl}-2-thienyl)methyl][3-(trifluoro-

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(({1-[(cyclohexylamino)carbonyl]-4-piperidinyl}methyl){4-[(dodecylamino)-
carbonyl] benzyl}amino)(oxo)acetic acid;
       ([(1-{[4-(dimethylamino)anilino]carbonyl}-4-piperidinyl)methyl]{4-[(dodecyl-amino)
carbonyl]benzyl}amino)(oxo)acetic acid;
        {{4-[(dodecylamino)carbonyl]benzyl}{(1-hexanoyl-4-piperidinyl)methyl]-amino}-
(oxo)acetic acid;
       ({4-[(dodecylamino)carbonyl]benzyl}{[1-(3-iodobenzoyl)-4-piperidinyl]methyl}-
amino)(oxo)acetic acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[(1-{(2E)-3-[3-(trifluoromethyl)phenyl]-2-
propenoyl}-4-piperidinyl)methyl]amino}(oxo)acetic acid;
       ({4-[(dodecylamino)carbonyl]benzyl}{[1-(2-quinoxalinylcarbonyl)-4-piperidinyl]-
methyl}amino)(oxo)acetic acid;
       [({1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}methyl)(4-{[(4-phenoxybenzyl)
amino]carbonyl}benzyl)amino](oxo)acetic acid;
       [{[1-(3-iodobenzoyl)-4-piperidinyl]methyl}(4-{[(4-phenoxybenzyl)aminol-carbonyl}
benzyl)amino](oxo)acetic acid;
       oxo{(4-{[(4-phenoxybenzyl)amino]carbonyl}benzyl)[(1-{(2E)-3-[3-(trifluoromethyl)
phenyl]-2-propenoyl}-4-piperidinyl)methyl]amino}acetic acid;
       {{4-[(dodecylamino)carbonyl]phenyl}[2-(methoxycarbonyl)benzyl]-amino}(oxo)
acetic acid;
       [[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2-bromobenzyl](4-iodobenzyl)-
amino](oxo)acetic acid;
       [(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)(4-iodobenzyl)amino]-(oxo)
acetic acid;
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[{2-bromo-4-[(dodecylamino)carbonyl]benzyl}(4-iodobenzyl)amino](oxo)acetic acid;

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benzyll amino}(oxo)acetic acid:

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[(2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)(4-iodobenzyl)amino]-
(oxo)acetic acid;
        ((4-iodobenzyl){[4'-({[2-(4-phenoxyphenyl)ethyl]amino}carbonyl)-1,1'-biphenyl-4-
yl] methyl}amino)(oxo)acetic acid;
        {[2-bromo-4-({[2-(4-phenoxyphenyl)ethyl]amino}carbonyl)benzyl][(4'-fluoro-1,1'-
biphenyl-3-yl)methyl]amino}(oxo)acetic acid;
        \{[4-(\{[2-(1,1'-biphenyl-4-yl)ethyl]amino\}carbonyl)-2-bromobenzyl][(4'-fluoro-1,1'-biphenyl-4-yl)ethyl]amino\}carbonyl)-2-bromobenzyl][(4'-fluoro-1,1'-biphenyl-4-yl)ethyl]amino}
biphenyl-3-yl)methyl]amino}(oxo)acetic acid;
        {(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[(4'-fluoro-1,1'-biphenyl-3-
yl) methyl]amino}(oxo)acetic acid;
        {[2,6-dibromo-4-({[2-(4-phenoxyphenyl)ethyl]amino}carbonyl)benzyl][(4'-fluoro-
1,1'-biphenyl-3-yl)methyl]amino}(oxo)acetic acid;
        {[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2,6-dibromobenzyl][(4'-fluoro-
1,1'-biphenyl-3-yl)methyl]amino}(oxo)acetic acid;
        {(2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[(4'-fluoro-1,1'-biphenyl-
3-yl)methyl]amino}(oxo)acetic acid;
        {{2,6-dibromo-4-[(dodecylamino)carbonyl]benzyl}[(4'-fluoro-1,1'-biphenyl-3-yl)
methyllamino (oxo) acetic acid:
       ([(4'-fluoro-1,1'-biphenyl-3-yl)methyl]{[4'-({[2-(4-phenoxyphenyl)ethyl]amino}-
carbonyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;
        {({4'-[(dodecylamino)carbonyl]-1,1'-biphenyl-4-yl}methyl)[(4'-fluoro-1,1'-biphenyl-
3-yl)methyl]amino}(oxo)acetic acid;
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{(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[2-(trifluoromethoxy)-

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{(2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[2-(trifluoromethoxy)-benzyl]amino}(oxo)acetic acid;

oxo{{[4'-({[2-(4-phenoxyphenyl)ethyl]amino}carbonyl)-1,1'-biphenyl-4-yl]methyl}-
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[2-(trifluoromethoxy)benzyl]amino}acetic acid;

{({4'-[(dodecylamino)carbonyl]-1,1'-biphenyl-4-yl}methyl)[2-(trifluoromethoxy)-benzyl]amino}(oxo)acetic acid;

[[2-bromo-4-({[2-(4-phenoxyphenyl)ethyl]amino}carbonyl)benzyl](3-phenoxybenzyl) amino](oxo)acetic acid;

[[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2-bromobenzyl](3-phenoxybenzyl) amino](oxo)acetic acid;

[(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)(3-phenoxybenzyl)-amino] (oxo)acetic acid;

[[2,6-dibromo-4-({[2-(4-phenoxyphenyl)ethyl]amino}carbonyl)benzyl](3-phenoxybenzyl)amino](oxo)acetic acid;

[[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2,6-dibromobenzyl](3-phenoxy-benzyl)amino](oxo)acetic acid;

[(2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)(3-phenoxybenzyl)-amino] (oxo)acetic acid;

[{2,6-dibromo-4-[(dodecylamino)carbonyl]benzyl}(3-phenoxybenzyl)amino](oxo)-acetic acid;

 $oxo((3-phenoxybenzyl)\{[4'-(\{[2-(4-phenoxyphenyl)ethyl]amino\}carbonyl)-1,1'-biphenyl-4-yl]methyl\}amino)acetic acid;$

oxo[[(4'-{[(4-pentylbenzyl)amino]carbonyl}-1,1'-biphenyl-4-yl)methyl](3-phenoxy benzyl)amino]acetic acid;

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[({4'-[(dodecylamino)carbonyl]-1,1'-biphenyl-4-yl}methyl)(3-phenoxybenzyl)-amino] (oxo)acetic acid;
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[[2-bromo-4-({[2-(4-phenoxyphenyl)ethyl]amino}carbonyl)benzyl](2-iodobenzyl)-amino](oxo)acetic acid;

[[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2-bromobenzyl](2-iodobenzyl)-amino](oxo)acetic acid;

[(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)(2-iodobenzyl)amino]-(oxo) acetic acid;

[{2-bromo-4-[(dodecylamino)carbonyl]benzyl}(2-iodobenzyl)amino](oxo)acetic acid ([2-bromo-4-({[2-(4-phenoxyphenyl)ethyl]amino}carbonyl)benzyl]{[2'-(trifluoromethyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;

([4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2-bromobenzyl]{[2'-(trifluoromethyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;

((2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl){[2'-(trifluoromethyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;

((2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl){[2'-(trifluoromethyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;

({2-bromo-4-[(dodecylamino)carbonyl]benzyl} {[2'-(trifluoromethyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;

([4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2,6-dibromobenzyl]{[2'-(tri-fluoromethyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;

((2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl){[2'-(trifluoromethyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;

({2,6-dibromo-4-[(dodecylamino)carbonyl]benzyl} {[2'-(trifluoromethyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;

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(({4'-[(dodecylamino)carbonyl]-1,1'-biphenyl-4-yl}methyl){[2'-(trifluoromethyl)-1,1'-biphenyl-4-yl]methyl}amino)(oxo)acetic acid;
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[[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2-bromobenzyl](1,1'-biphenyl-2-ylmethyl)amino](oxo)acetic acid;

[(1,1'-biphenyl-2-ylmethyl)(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)-amino](oxo)acetic acid;

((1,1'-biphenyl-2-ylmethyl){2-bromo-4-[(dodecylamino)carbonyl]benzyl}-amino)(oxo)acetic acid;

{(1,1'-biphenyl-2-ylmethyl)[2,6-dibromo-4-({[2-(4-phenoxyphenyl)ethyl]amino}-carbonyl)benzyl]amino}(oxo)acetic acid;

[[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2,6-dibromobenzyl](1,1'-biphenyl-2-ylmethyl)amino](oxo)acetic acid;

[(1,1'-biphenyl-2-ylmethyl)(2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}-benzyl)amino](oxo)acetic acid;

((1,1'-biphenyl-2-ylmethyl){2,6-dibromo-4-[(dodecylamino)carbonyl]benzyl}-amino) (oxo)acetic acid;

{(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[4-(trifluoromethoxy)-benzyl]amino}(oxo)acetic acid;

{{2-bromo-4-[(dodecylamino)carbonyl]benzyl}[4-(trifluoromethoxy)benzyl]amino}(oxo)acetic acid;

{(2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[4-(trifluoromethoxy)-benzyl]amino}(oxo)acetic acid;

{(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[3-(trifluoromethoxy)-benzyl] amino}(oxo)acetic acid;

{{2-bromo-4-[(dodecylamino)carbonyl]benzyl}[3-(trifluoromethoxy)benzyl]amino}-{(2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[3-(trifluoromethoxy)-{{2,6-dibromo-4-[(dodecylamino)carbonyl]benzyl}[3-(trifluoromethoxy)benzyl]-{({4'-[(dodecylamino)carbonyl]-1,1'-biphenyl-4-yl}methyl)[3-(trifluoromethoxy)-[[2-bromo-4-({[2-(4-phenoxyphenyl)ethyl]amino}carbonyl)benzyl](4-phenoxy-[[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2-bromobenzyl](4-phenoxy-[(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)(4-phenoxybenzyl)-amino] (oxo)acetic acid; [{2-bromo-4-[(dodecylamino)carbonyl]benzyl}(4-phenoxybenzyl)amino](oxo)acetic acid; [[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2,6-dibromobenzyl](4-phenoxybenzyl)amino](oxo)acetic acid; [(2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)(4-phenoxybenzyl)amino] (oxo)acetic acid; {[4-({[2-(1,1'-biphenyl-4-yl)ethyl]amino}carbonyl)-2-bromobenzyl][4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid; {(2-bromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[4-(trifluoromethyl)-benzyl]-

amino}(oxo)acetic acid;

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Appeal Brief
       {{2-bromo-4-[(dodecylamino)carbonyl]benzyl}[4-(trifluoromethyl)benzyl]amino}-
(oxo)acetic acid;
       {(2,6-dibromo-4-{[(4-pentylbenzyl)amino]carbonyl}benzyl)[4-(trifluoromethyl)-
benzyl]amino}(oxo)acetic acid;
       {{2,6-dibromo-4-[(dodecylamino)carbonyl]benzyl}[4-(trifluoromethyl)benzyl]-
amino) (oxo)acetic acid;
       oxo{[(4'-{[(4-pentylbenzyl)amino]carbonyl}-1,1'-biphenyl-4-yl)methyl][4-(trifluoro-
methyl)benzyl]amino}acetic acid;
       {{2-bromo-4-[(dodecylamino)carbonyl]benzyl}[3-(trifluoromethyl)benzyl]-
amino}(oxo)acetic acid;
       {{2,6-dibromo-4-[(dodecylamino)carbonyl]benzyl}[3-(trifluoromethyl)benzyl]-
amino) (oxo)acetic acid;
       oxo{[(4'-{[(4-pentylbenzyl)amino]carbonyl}-1,1'-biphenyl-4-yl)methyl][3-(trifluoro
methyl)benzyl]amino}acetic acid;
       {(4-dibenzo[b,d]furan-4-ylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;
       {(4-dibenzo[b,d]furan-4-ylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid,
N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       ({4-[(dodecylamino)carbonyl]benzyl}{1-[4-(trifluoromethyl)phenyl]ethyl}amino)-
(oxo)acetic acid;
       ({4-[(dodecylamino)carbonyl]benzyl}{1-[4-(trifluoromethyl)phenyl]ethyl}amino)-
(oxo)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {({4'-[(octylamino)carbonyl]-1,1'-biphenyl-4-yl}methyl)[4-(trifluoromethyl)benzyl]-
amino}(oxo)acetic acid;
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oxo{(4-tetradec-1-ynylbenzyl)[4-(trifluoromethyl)benzyl]amino}acetic acid;

{(4-dodec-1-ynylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;

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{{4-[(dodecylamino)carbonyl]benzyl}[4-(trifluoromethyl)phenyl]amino}(oxo)acetic
acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(2-methoxyphenyl)amino](oxo)acetic acid;
       ((1,2-diphenylethyl){4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       N-(carboxycarbonyl)-N-{4-[(dodecylamino)carbonyl]benzyl}-L-phenylalanine;
       [{4-[(dodecylamino)carbonyl]benzyl}(3-phenoxyphenyl)amino](oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(2-isopropoxyphenyl)amino](oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(4-iodophenyl)amino](oxo)acetic acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[3-fluoro-4-(trifluoromethyl)benzyl]-amino}
(oxo)acetic acid;
       ((3-chloro-2-methylphenyl){4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid:
       4'-((carboxycarbonyl){4-[(dodecylamino)carbonyl]benzyl}amino)-1,1'-biphenyl-2-
carboxylic acid;
       ((2,4-dichlorobenzyl){4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(1-phenylpropyl)amino](oxo)acetic acid;
       ([2-(4-chlorophenyl)propyl]{4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid;
       [{4-[(dodecylamino)carbonyl]benzyl}(4-isopropoxyphenyl)amino](oxo)acetic acid;
       ([4-(benzyloxy)phenyl]{4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[2-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid:
       [{4-[(dodecylamino)carbonyl]benzyl}(2-methoxybenzyl)amino](oxo)acetic acid;
       ([(1R)-1-(4-chlorophenyl)ethyl]{4-[(dodecylamino)carbonyl]benzyl}amino)-(oxo)
acetic acid;
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(oxo)acetic acid;

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((3,4-dichlorobenzyl) {4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid
      ((1-benzothien-3-ylmethyl){4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid;
       ([2-(2,6-dichlorophenyl)ethyl]{4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic
acid;
       ({4-[(dodecylamino)carbonyl]benzyl}{2-[3-(trifluoromethyl)phenyl]ethyl}-amino)-
(oxo)acetic acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[2-(3-fluorophenyl)ethyl]amino}(oxo)acetic
acid;
       ([(1S)-1-(4-chlorophenyl)ethyl]{4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)-
acetic acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[(1S)-1-phenylethyl]amino}(oxo)acetic acid;
       {{4-[(dodecylamino)carbonyl]benzyl}[(1R)-1-phenylethyl]amino}(oxo)acetic acid;
       ([3-(benzyloxy)phenyl]{4-[(dodecylamino)carbonyl]benzyl}amino)(oxo)acetic acid;
       N-(carboxycarbonyl)-N-{4-[(dodecylamino)carbonyl]benzyl}-D-phenylalanine;
       {{4-[(dodecylamino)carbonyl]phenyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
       {{4-[(dodecylamino)carbonyl]phenyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       oxo{{1-[4-(trifluoromethyl)phenyl]ethyl}[4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]
amino}acetic acid;
       oxo{{1-[4-(trifluoromethyl)phenyl]ethyl}[4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]
amino}acetic acid. N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       ([(2-butyl-1-benzofuran-3-yl)methyl]{4-[(dodecylamino)carbonyl]benzyl}-amino)
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salt;

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{(1-{4-[(dodecylamino)carbonyl]phenyl}ethyl)[4-(trifluoromethyl)benzyl]amino}-
       {(1-{4-[(dodecylamino)carbonyl]phenyl}ethyl)[4-(trifluoromethyl)benzyl]amino}-
(oxo)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {(4-{[(4-octylphenyl)amino]carbonyl}benzyl)[4-(trifluoromethyl)benzyl]-
amino}(oxo) acetic acid;
       {(3-chlorobenzyl)[4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic acid;
       {(3-chlorobenzyl)[4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic acid,
N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {{cyclopentyl[4-(trifluoromethyl)phenyl]methyl}[4-(tridecanoylamino)benzyl]-
amino}(oxo)acetic acid;
       oxo([4-(trifluoromethyl)benzyl]{[4-(3-undecyl-1,2,4-oxadiazol-5-yl)-1-naphthyl]-
methyl amino) acetic acid;
       oxo([4-(trifluoromethyl)benzyl]{[4-(3-undecyl-1,2,4-oxadiazol-5-yl)-1-naphthyl]-
methyl}amino)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)-glucitol)
       {{cyclopentyl[4-(trifluoromethyl)phenyl]methyl}[4-(3-undecyl-1,2,4-oxadiazol-5-
yl)benzyl]amino}(oxo)acetic acid;
       {{cyclopentyl[4-(trifluoromethyl)phenyl]methyl}[4-(3-undecyl-1,2,4-oxadiazol-5-
yl)benzyl]amino}(oxo)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methyl-
amino)glucitol) salt;
       {(4-dibenzo[b,d]furan-4-ylphenyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;
        {(4-dibenzo[b,d]furan-4-ylphenyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid,
N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
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{[4-(octyloxy)benzyl][4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;

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{[4-(octyloxy)benzyl][4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid, N-methyl-
D-glucamine (i.e.1-deoxy-1-(methylamino)glucitol) salt;
       [[2-(3-chlorophenyl)ethyl](4-dec-1-ynylbenzyl)amino](oxo)acetic acid;
       ([2-(3-chlorophenyl)ethyl]{4-[(1Z)-dec-1-enyl]benzyl}amino)(oxo)acetic acid;
       {[2-(3-chlorophenyl)ethyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)-
acetic acid;
       {[2-(3-chlorophenyl)ethyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)-
acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       oxo{{(1R)-1-[4-(trifluoromethyl)phenyl]ethyl}[4-(3-undecyl-1,2,4-oxadiazol-5-
yl)benzyl]amino}acetic acid;
       oxo{{(1R)-1-[4-(trifluoromethyl)phenyl]ethyl}[4-(3-undecyl-1,2,4-oxadiazol-5-
yl)benzyl]amino}acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)-glucitol)
salt;
       oxo{[4-(trifluoromethyl)phenyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-
acetic acid;
       oxo{[4-(trifluoromethyl)phenyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-
acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       oxo{{(1S)-1-[4-(trifluoromethyl)phenyl]ethyl}[4-(3-undecyl-1,2,4-oxadiazol-5-
yl)benzyl]amino}acetic acid;
       oxo { ((1S)-1-[4-(trifluoromethyl)phenyl]ethyl} [4-(3-undecyl-1,2,4-oxadiazol-5-
yl)benzyl]amino}acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)-glucitol)
salt;
       [(3-chlorobenzyl)(4-dec-1-ynylbenzyl)amino](oxo)acetic acid;
       [(3-chlorobenzyl)(4-dec-1-ynylbenzyl)amino](oxo)acetic acid, N-methyl-D-
glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
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       [[2-(3-chlorophenyl)ethyl](4-oct-1-ynylbenzyl)amino](oxo)acetic acid;
       [[2-(3-chlorophenyl)ethyl](4-oct-1-ynylbenzyl)amino](oxo)acetic acid, N-methyl-D-
glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {(4-dec-1-ynylbenzyl)[4-(trifluoromethyl)phenyl]amino}(oxo)acetic acid;
       ((4-dec-1-ynylbenzyl){1-[4-(trifluoromethyl)phenyl]ethyl}amino)(oxo)acetic acid;
       ((4-dec-1-ynylbenzyl){1-[4-(trifluoromethyl)phenyl]ethyl}amino)(oxo)acetic acid, N-
methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {{1-methyl-1-[4-(trifluoromethyl)phenyl]ethyl}[4-(3-undecyl-1,2,4-oxadiazol-5-yl)
benzyl]amino}(oxo)acetic acid;
       {{1-methyl-1-[4-(trifluoromethyl)phenyl]ethyl}[4-(3-undecyl-1,2,4-oxadiazol-5-yl)
benzyl]amino}(oxo)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-
(methylamino)glucitol) salt; {[2-(3-chlorophenyl)ethyl][4-(3-octyl-1,2,4-oxadiazol-5-
yl)benzyl]amino}(oxo)acetic acid;
       {[2-(3-chlorophenyl)ethyl][4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic
acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {[4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl][4-(trifluoromethyl)benzyl]amino}-(oxo)
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acetic acid; {[4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl][4-(trifluoromethyl)benzyl]amino}-(oxo)-

acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;

{{[4-(dodecyloxy)-1-naphthyl]methyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;

{{[4-(dodecyloxy)-1-naphthyl]methyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt[(4-bromobenzyl)(4oct-1-ynylbenzyl)amino](oxo)acetic acid;

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[{4-[(dodecylamino)carbonyl]benzyl}(2-hydroxy-1-phenylethyl)amino](oxo)acetic
acid;
       ((4-dec-1-ynylbenzyl){1-methyl-1-[4-(trifluoromethyl)phenyl]ethyl}amino)(0x0)-
acetic acid;
       ((4-dec-1-ynylbenzyl){1-methyl-1-[4-(trifluoromethyl)phenyl]ethyl}amino)(oxo)-
acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       oxo\{\{4-[(9Z)-tetradec-9-enoylamino]benzyl\}[4-(trifluoromethyl)benzyl]amino\}-
acetic acid;
       {(4-dec-1-ynylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;
       oxo{[4-(trifluoromethyl)benzyl][3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]-
amino}acetic acid;
       oxo{[4-(trifluoromethyl)benzyl][3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-
acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {(4-dodecylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;
       ((4-dodecylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid, N-methyl-D-
glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {[4-({[(2-butyl-1-benzofuran-3-yl)methyl]amino}carbonyl)benzyl][4-(trifluoro-
methyl)benzyl]amino}(oxo)acetic acid;
       {(4-{[4-(benzyloxy)benzoyl]amino}benzyl)[4-(trifluoromethyl)benzyl]amino}-(oxo)
acetic acid;
       {(3,5-dichlorobenzyl)[4-(tridecanoylamino)benzyl]amino}(oxo)acetic acid;
       {(3,5-dichlorobenzyl)[4-(tridecanoylamino)benzyl]amino}(oxo)acetic acid, N-methyl
-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {{4-[(4-octylphenyl)ethynyl]benzyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
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oxo{[4-(trifluoromethyl)benzyl][4-(5-undecyl-1,2,4-oxadiazol-3-yl)benzyl]amino}-
acetic acid:
       oxo{[4-(trifluoromethyl)benzyl][4-(5-undecyl-1,2,4-oxadiazol-3-yl)benzyl]amino}-
acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       \{\{4-[2-(4-octylphenyl)ethyl]benzyl\}[4-(trifluoromethyl)benzyl]amino\}(oxo)acetic
acid;
       {(4-{[4-(heptyloxy)phenyl]ethynyl}benzyl)[4-(trifluoromethyl)benzyl]amino}-
(oxo)acetic acid;
       \{\{4\hbox{-}[(4\hbox{-}butylphenyl)ethynyl]benzyl}\}[4\hbox{-}(trifluoromethyl)benzyl]amino}\}(oxo)acetic
acid;
        \{\{4-[(4-hexylphenyl)ethynyl]benzyl\}[4-(trifluoromethyl)benzyl]amino\}(oxo)acetic
acid;
        \{\{4-[(4-hexylphenyl)ethynyl]benzyl\}[4-(trifluoromethyl)benzyl]amino\}(oxo)acetic
acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
        oxo{(4-{[4-(pentyloxy)phenyl]ethynyl}benzyl)[4-(trifluoromethyl)benzyl]-amino}-
acetic acid;
        oxo\{\{4\hbox{-}[(4\hbox{-propylphenyl})ethynyl]benzyl\}[4\hbox{-}(trifluoromethyl)benzyl]amino}\} acetic
acid;
        [[2-(3-chlorophenyl)ethyl](4-dodec-1-ynylbenzyl)amino](oxo)acetic acid;
        [[2-(3-chlorophenyl)ethyl](4-dodec-1-ynylbenzyl)amino](oxo)acetic acid, N-methyl-
D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
        {(4-oct-1-ynylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;
        \{[4\hbox{-}(11\hbox{-hydroxyundec-1-ynyl})benzyl][4\hbox{-}(trifluoromethyl)benzyl]amino}\} (oxo) acetic
 acid;
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{[4-(11-methoxy-11-oxoundec-1-ynyl)benzyl][4-(trifluoromethyl)benzyl]amino}-
(oxo)acetic acid;
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11-[4-({(carboxycarbonyl)[4-(trifluoromethyl)benzyl]amino}methyl)phenyl]undec10-ynoic acid;

{(4-{[4-(benzyloxy)phenyl]ethynyl}benzyl)[4-(trifluoromethyl)benzyl]amino}-(oxo) acetic acid;

{(4-{2-[4-(heptyloxy)phenyl]ethyl}benzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)-acetic acid;

{{4-[2-(4-butylphenyl)ethyl]benzyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;

{{4-[2-(4-hexylphenyl)ethyl]benzyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;

{{4-[2-(4-hexylphenyl)ethyl]benzyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;

oxo{(4-{2-[4-(pentyloxy)phenyl]ethyl}benzyl)[4-(trifluoromethyl)benzyl]-amino} acetic acid;

 $oxo\{\{4-[2-(4-propylphenyl)ethyl]benzyl\}[4-(trifluoromethyl)benzyl]amino\} acetic acid;$

11-[4-({(carboxycarbonyl)[4-(trifluoromethyl)benzyl]amino}methyl)phenyl]-undecanoic acid;

{[4-(11-hydroxyundecyl)benzyl][4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid; {(4-dodec-1-ynylbenzyl)[4-(trifluoromethyl)phenyl]amino}(oxo)acetic acid; {(4-dodec-1-ynylbenzyl)[4-(trifluoromethyl)phenyl]amino}(oxo)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;

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oxo([4-(trifluoromethyl)benzyl]{4-[2-(3-undecyl-1,2,4-oxadiazol-5-yl)ethyl]benzyl}-
amino)acetic acid;
       oxo([4-(trifluoromethyl)benzyl]{4-[2-(3-undecyl-1,2,4-oxadiazol-5-yl)ethyl]benzyl}-
amino)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {{4-[2-(3-octyl-1,2,4-oxadiazol-5-yl)ethyl]benzyl}[4-(trifluoromethyl)benzyl]-
amino} (oxo)acetic acid;
       {\{4-[2-(3-octyl-1,2,4-oxadiazol-5-yl)ethyl]benzyl}[4-(trifluoromethyl)benzyl]-
amino}(oxo)acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino) glucitol) salt;
       {{4-[(4-octylbenzoyl)amino]benzyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
       {{4-[(4-octylbenzoyl)amino]benzyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       oxo{[(1-tridecanoylpiperidin-4-yl)methyl][4-(trifluoromethyl)benzyl]amino}acetic
acid;
       {{[1-(4-octylbenzoyl)piperidin-4-yl]methyl}[4-(trifluoromethyl)benzyl]-amino}-
(oxo)acetic acid;
       {{[1-(4-octylbenzoyl)piperidin-4-yl]methyl}[4-(trifluoromethyl)benzyl]amino}-(oxo)
acetic acid, N-methyl-D-glucamine (i.e. 1-deoxy-1-(methylamino)glucitol) salt;
       {[(3-dec-1-ynyl-1-benzofuran-5-yl)methyl][4-(trifluoromethyl)benzyl]amino}-(oxo)
acetic acid;
        {[(3-dodec-1-ynyl-1-benzofuran-5-yl)methyl][4-(trifluoromethyl)benzyl]amino}-
(oxo) acetic acid;
       oxo{({3-[(4-propylphenyl)ethynyl]-1-benzofuran-5-yl}methyl)[4-(trifluoromethyl)-
benzyl]amino}acetic acid;
       [(4-dodec-1-ynylbenzyl)(4-fluorobenzyl)amino](oxo)acetic acid;
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[bis(4-oct-1-ynylbenzyl)amino](oxo)acetic acid;
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{[(6-dodec-1-ynylpyridin-3-yl)methyl][4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;

 $\{(3\text{-}dodec\text{-}1\text{-}ynylbenzyl)[4\text{-}(trifluoromethyl)benzyl]amino}\} (oxo) acetic acid;$

{[2-(2-fluorophenyl)ethyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-(oxo) acetic acid;

{[2-(2-fluorophenyl)ethyl][3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-(oxo) acetic acid;

{[2-(2-fluorophenyl)ethyl][4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic acid;

{[2-(3,4-dichlorophenyl)ethyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic acid;

{[2-(3,4-dichlorophenyl)ethyl][3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic acid;

{[2-(3,4-dichlorophenyl)ethyl][4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl] amino}(oxo)acetic acid;

{[2-(1,1'-biphenyl-4-yl)ethyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo) acetic acid;

{[2-(1,1'-biphenyl-4-yl)ethyl][3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo) acetic acid;

{[2-(1,1'-biphenyl-4-yl)ethyl][4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-(oxo) acetic acid;

oxo{5,6,7,8-tetrahydronaphthalen-1-yl[4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]-amino}acetic acid;

oxo{5,6,7,8-tetrahydronaphthalen-1-yl[3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]-amino}acetic acid;

[[4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl](5,6,7,8-tetrahydronaphthalen-1-yl)amino](oxo)acetic acid;

{(1,1'-biphenyl-3-ylmethyl)[4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-(oxo) acetic acid;

{(1,1'-biphenyl-3-ylmethyl)[3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-(oxo) acetic acid;

{(1,1'-biphenyl-3-ylmethyl)[4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-(oxo)-acetic acid;

{(1-benzothien-3-ylmethyl)[4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-(oxo)-acetic acid;

{(1-benzothien-3-ylmethyl)[3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)-acetic acid;

{(1-benzothien-3-ylmethyl)[4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)-acetic acid;

oxo{[2-(trifluoromethyl)benzyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}-acetic acid;

oxo{[2-(trifluoromethyl)benzyl][3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino} acetic acid;

{[4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl][2-(trifluoromethyl)benzyl]amino}(oxo)-acetic acid;

oxo{[3-(trifluoromethyl)benzyl][4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]-amino}-acetic acid;

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oxo{[3-(trifluoromethyl)benzyl][3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]-amino}-
acetic acid;
       {[4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl][3-(trifluoromethyl)benzyl]amino}-(oxo)-
acetic acid;
       {(2-methoxybenzyl)[4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic
acid {(2-methoxybenzyl)[3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)-acetic acid;
       {(2-methoxybenzyl)[4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic acid;
       oxo{{4-[(trifluoromethyl)sulfonyl]benzyl}[4-(3-undecyl-1,2,4-oxadiazol-5-yl)-
benzyl] amino} acetic acid;
       oxo{{4-[(trifluoromethyl)sulfonyl]benzyl}[3-(3-undecyl-1,2,4-oxadiazol-5-yl)-
benzyl] amino} acetic acid;
       ([4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl]{4-[(trifluoromethyl)-sulfonyl]benzyl}-
amino)(oxo)acetic acid;
       {1,3-benzodioxol-5-yl[4-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic
acid;
       {1,3-benzodioxol-5-yl[3-(3-undecyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic
acid;
       {1,3-benzodioxol-5-yl[4-(3-octyl-1,2,4-oxadiazol-5-yl)benzyl]amino}(oxo)acetic
acid;
       {[(4-dodec-1-ynyl-1-naphthyl)methyl][4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
        {[(4-dec-1-ynyl-1-naphthyl)methyl][4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
        {[(4-dec-1-ynyl-1-naphthyl)methyl][4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
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oxo{[4-(trifluoromethyl)benzyl][4-(4-undecyl-1,3-thiazol-2-yl)benzyl]amino}acetic
acid;
       {(4-dec-1-ynylbenzyl)[2-(2-fluorophenyl)ethyl]amino}(oxo)acetic acid;
       {(4-dodec-1-ynylbenzyl)[2-(2-fluorophenyl)ethyl]amino}(oxo)acetic acid;
       {{[4-(dodecyloxy)-1-naphthyl]methyl}[2-(2-fluorophenyl)ethyl]amino}(oxo)acetic
acid;
       {[2-(2-fluorophenyl)ethyl][4-(octyloxy)benzyl]amino}(oxo)acetic acid;
       {(4-dec-1-ynylbenzyl)[2-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;
       {(4-dodec-1-ynylbenzyl)[2-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;
       {{[4-(dodecyloxy)-1-naphthyl]methyl}[2-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
       {[4-(octyloxy)benzyl][2-(trifluoromethyl)benzyl]amino}(oxo)acetic acid;
       {(4-dec-1-ynylbenzyl)[2-(3,4-dichlorophenyl)ethyl]amino}(oxo)acetic acid;
       [[2-(3,4-dichlorophenyl)ethyl](4-dodec-1-ynylbenzyl)amino](oxo)acetic acid;
       ([2-(3,4-dichlorophenyl)ethyl]{[4-(dodecyloxy)-1-naphthyl]methyl}amino) (oxo)
acetic acid;
       {[2-(3,4-dichlorophenyl)ethyl][4-(octyloxy)benzyl]amino}(oxo)acetic acid;
       ({4-[(4-hexylphenyl)ethynyl]benzyl}{1-methyl-1-[4-(trifluoromethyl)phenyl] ethyl}
amino)(oxo)acetic acid;
       {[4-(5-cyclohexylpent-1-ynyl)benzyl][4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
       {{3-[(4-hexylphenyl)ethynyl]benzyl}[4-(trifluoromethyl)benzyl]amino}(oxo)acetic
acid;
       {[4-(4-ethyl-3-hydroxyoct-1-ynyl)benzyl][4-(trifluoromethyl)benzyl]amino}-(oxo)-
acetic acid;
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{(2-dec-1-ynylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid; {(4-dec-1-ynylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid, L-lysine salt;

{(4-dec-1-ynylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid, tromethamine (i.e. (2-amino-2-hydroxymethyl)-1,3-propanediol) salt;

{(4-dec-1-ynylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetic acid, L-Arginine salt; and

sodium {(4-dec-1-ynylbenzyl)[4-(trifluoromethyl)benzyl]amino}(oxo)acetate.

Claims 17-19 (Cancelled).

- 20. (Rejected) The method according to claim 1, wherein coronary obstruction is treated.
- 21. (Rejected) The method according to claim 1, wherein peripheral vasoconstriction is treated.

EVIDENCE APPENDIX

None

RELATED PROCEEDINGS APPENDIX

None.